

AMENDMENTS TO THE SPECIFICATION:

Further to the Supplemental Amendment filed on April 22, 2002, please replace the paragraphs beginning on pages 15-18 as follows:

Page 15, please replace the paragraph beginning on line 22 with the following amended paragraph:

--The isotopic ratios  $R(i)$  are expressed in deviations  $\delta(i)$  ‰ relative to an international reference  $R(\text{ref})$  by means of the relationship:

$$\delta(i) = ((R(i)/R(\text{ref}))-1)*1000$$

$^2\text{H}$  and  $^{18}\text{O}$ : V. SMOW (Vienna-Standard Mean Ocean Water)

$^{13}\text{C}$ : V.PDB (Vienna-Pee Dee Belemnite)

$^{15}\text{N}$ : atmospheric nitrogen

$^{34}\text{S}$ : CDT, specimen of Troilite extracted from Diablo Canyon (USA)--

Page 16, please replace the paragraph beginning on line 7, with the following amended paragraph:

--The benzene rings of fossil origin (petroleum) are characterized by values of  $\delta$   $^2\text{H}$  comprised between -20 and -120 ‰ and the saturated side chains between 0 and -70. Measurements are carried out by NMR (SNIF-NMR) for the side chains and the overall content by Mass Spectrometry (MSIR). The overall contents in  $^{13}\text{C}$  measured by MSIR are generally equal to -28.5 ‰ with a typical variation of the order of 2 ‰ and the isotopic contents of  $^{13}\text{C}$  of the alkylated or

functional side chains are measured by NMR. According to the synthesis process and the origin of the primary material of the side chains, the values  $\delta^{13}\text{C}$  can vary between -5 and -100 ~~0/00~~ 0/00 and thus offer an important characterization potential.--

Page 16, please replace the paragraph beginning on line 20 with the following amended paragraph:

--Nitrated molecules of synthetic origin have  $^{13}\text{C}$  and  $^{15}\text{N}$  values, measured by MSIR, which are relatively low and equal respectively to -30 ~~0/00~~ 0/00 (1.5) and -20 ~~0/00~~ 0/00 (10) but, in this latter case, the cyclization reactions of pyrazoles and xanthines lead to substantial impoverishment in heavy isotopes. At this level, it can be considered that the values of  $\delta^{15}\text{N}$  of the CN group or of the  $\text{CONH}_2$  group reflect those of the primary materials because the introduction into the 1H-pyrazole pattern takes place without significant isotopic fractionation. The content in  $^{15}\text{N}$  of the  $\text{NH}_2$  group is all the lower relative to that of the primary material, the lower is the yield of the reaction.--

Page 17, please replace the paragraph beginning on line 15 with the following amended paragraph:

--Finally, it is interesting to note that the isotopic mapping of citric acid is very well defined and that the origin of the sildenafil citrate can be precisely determined by consideration of the isotopic distribution in the citrate fragment. Thus, the content of  $^2\text{H}$  measured by NMR varies between

-40 and -80 ~~0/00~~ 0/00 for biotechnological citric acids but the values  $\delta^{13}\text{C}$  are equal respectively to -11 ~~0/00~~ 0/00 (1) or -25 ~~0/00~~ 0/00 (1) accordingly as the primary material is constituted by a C34 or C3 sugar. The natural citric acids extracted from fruits such as citrus, pineapple or red fruits have  $\delta^2\text{H}$  values that are very near to 0 ~~0/00~~ 0/00 (25).--

Page 18, please replace the paragraph beginning on line 23 with the following amended paragraph:

--The  $\text{O}-\text{C}_2\text{H}_5$  group is naturally marked with  $^2\text{H}$ ,  $^{13}\text{C}$  or  $^{18}\text{O}$  from suitably chosen ethanol molecules. An ethanol synthesis has  $^2\text{H}$  values equal respectively to -100 and -160 ~~0/00~~ 0/00 at the two  $\text{CH}_3$  and  $\text{CH}_2$  sites with  $^{13}\text{C}$  contents of the order of -28 to -31 ~~0/00~~ 0/00 and  $^{18}\text{O}$  contents equal to -5-10 ~~0/00~~ 0/00. Moreover, a natural ethanol could have  $^2\text{H}$ ,  $^{13}\text{C}$ , or  $^{18}\text{O}$  contents equal respectively to -200 and -400 ~~0/00~~ 0/00 ( $^2\text{H}$ ), -11 ~~0/00~~ 0/00 ( $^{13}\text{C}$ ) and +7/+10 ( $^{18}\text{O}$ ). These two types of commercially available ethoxy groups without enriched addition, are easily introduced into the o-hydroxybenzoic acid molecule by means of conventional reactions to form the primary material P(-4b). The isotopic characteristics of this primary material, which become a typical fragment as described above, are present in the final molecule of sildenafil citrate.--

Page 4, replace the paragraph beginning on line 9 with the following amended paragraph:

--Correspondingly, more powerful analytic techniques have been developed. Such is the case of the mass spectrometry of isotopic ratios (MSIR). Thus, it is possible to characterize the natural specific isotopic fractionation by Nuclear Magnetic Resonance ~~(NMR-FINS method)~~ Specific Natural Isotope Fractionation (NMR-SNIF method) by measuring the isotopic contents at several molecular sites (or even all the sites) of a molecule. However, this technique is at present used only for simple molecules that can be directly analyzed.--